Amendments to the Specification

Please replace paragraph **[0019]** with the following amended paragraph:

[0019] PYK2 is also known as Cell Adhesion Kinase β (CAK β) and Related Adhesion Focal Tyrosine Kinase (RAFTK). Nucleotide and amino acid sequences for PYK2 are described in a set of related patents, including U.S. Patent ~~8,837,815~~ 5,837,815; 5,837,524; and Patent Publication U.S. 2002/0048782, which also provided additional information on PYK2 and a related protein, FAK, including some of the information described below. Each of these documents describes nucleotide and amino acid sequences for PYK2. Patent 5,837,524 describes a method of screening for agents "able to promote or disrupt the interaction" between "a PYK2 polypeptide and a natural binding partner (NBP)." (Col. 8, lines 60-67.) Patent Publication U.S. 2002/0048782 provides examples describing cloning and the testing of certain properties of PYK2. Each of these patents and patent publication are incorporated by reference herein in their entireties, including drawings.

Please replace paragraph **[0051]** with the following paragraph:

[0051] As used herein in connection with test compounds, binding compounds, and modulators (ligands), the term "synthesizing" and like terms means chemical synthesis from one or more precursor materials.

Please add the following new paragraphs after paragraph **[0146]**:

[0146.1] FIGURE 2 provides the multi-cloning site of the pET15S vector (SEQ ID NO: 7), including the sequence encoding the N-terminal hexa-histidine tag (peptide shown in SEQ ID NO: 8).

[0146.2] FIGURE 3 provides an alignment of kinase domains for several kinases, including human PYK2, providing identification of residues conserved between various members of the set

(residues 21-293 of SEQ ID NO: 2 and SEQ ID NOS 9-21, respectively, in order of appearance). The residue number is for PYK2.

[0146.3] The multiple panels of FIGURE 4 provide the nucleic acid and amino acid sequences for human PYK2 kinase domain (GenBank accession number U33284). FIGURE 4A provides the sequence of the full-length protein in pET15S (SEQ ID NO: 2), Mass: 33872.2, pI: 6.07, PYK2 kinase domain I420-M691 (SEQ ID NO: 1, subset of sequence shown minus first 21 amino acids). FIGURE 4B presents a PCR primer SEQ ID NO: 5. FIGURE 4C presents a PCR primer SEQ ID NO: 6. FIGURE 4D presents pET15S sequence PCR product (SEQ ID NO: 4), with sequence encoding PYK2 kinase domain in small letters (SEQ ID NO: 3).

Please replace paragraph **[0148]** with the following amended paragraph:

[0148] Table 1 provides atomic coordinates for human PYK2 kinase domain **(SEQ ID NO: 26)**. In this table and in Table 2, the various columns in the lines beginning with "ATOM" have the following content, beginning with the left-most column:
ATOM: Refers to the relevant moiety for the table row.
Atom number: Refers to the arbitrary atom number designation within the coordinate table.
Atom Name: Identifier for the atom present at the particular coordinates.
Chain ID: Chain ID refers to one monomer of the protein in the crystal, *e.g.*, chain "A", or to other compound present in the crystal, e.g., HOH for water, and L for a ligand or binding compound. Multiple copies of the protein monomers will have different chain Ids.
Residue Number: The amino acid residue number in the chain.
X, Y, Z: Respectively are the X, Y, and Z coordinate values.
Occupancy: Describes the fraction of time the atom is observed in the crystal. For example, occupancy = 1 means that the atom is present all the time; occupancy = o.5 indicates that the atom is present in the location 50% of the time.
B-factor: A measure of the thermal motion of the atom.
Element: Identifier for the element.

Please replace paragraph **[0150]** with the following amended paragraph:

[0150] Table 2 provides atomic coordinates for PYK2 **(SEQ ID NO: 26)** with (5'-adenylylimidodiphosphate) AMPPNP in the binding site.

Please delete paragraph **[0151]**.

Please delete paragraph **[0152]**.

Please replace paragraph **[0153]** with the following amended paragraph.

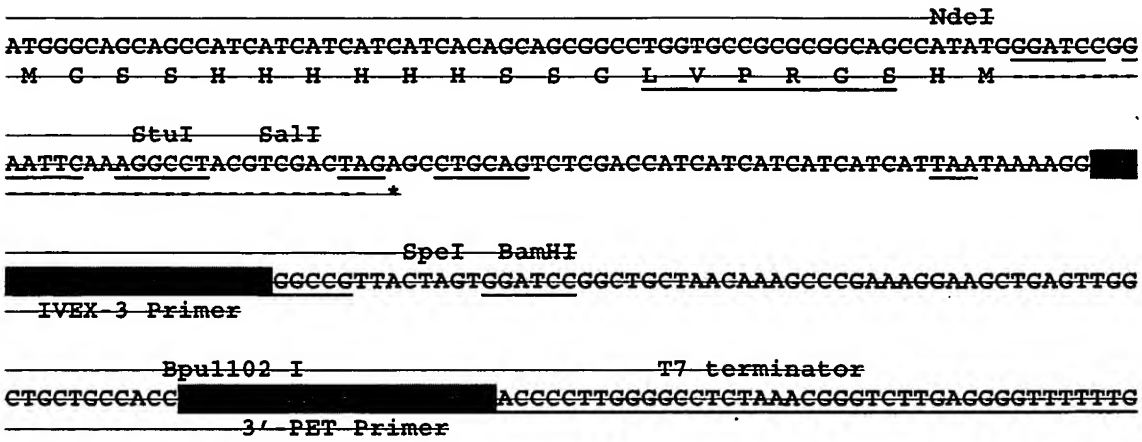
[0001] Table **[[5]]3** provides representative assay results for kinase activity of PYK2 kinase domain in the presence of ATP and in the presence of several ATP analogs.

Please replace paragraph **[0366]** with the following amended paragraph:

[0366] Kinase domain of PYK2 (amino acids 420 – 691**, SEQ ID NO: 1**) was amplified by polymerase chain reaction (PCR) using the specific primers 5'-TCCACAGCATATGATTGCCCGTGAAGA TGTGGT-3' (SEQ ID NO: 5) and 5'-CTCTCGTCGACCTACATGGCAATGTCCTTCTCCA-3' (SEQ ID NO: 6). The resulting PCR fragment was digested with *Nde*I and *Sal*I and was ligated into a modified pET15b vector (Novagen) with a cleavable N-terminal hexa-histidine tag (designated pET1S). PYK2 coding sequence has been deposited with GenBank under accession number U33284. A desired PYK2 sequence can be obtained using PCR with a brain (*e.g.*, human brain) cDNA library, such as obtaining kinase domain using the above primers in PCR. The multi-cloning site of the pET15S vector is shown in ~~the following sequence~~ **Figure 2** (SEQ ID NO: 7), including the sequence encoding the N-terminal ~~hexa-histadine~~ **hexa-histidine** tag (peptide shown in SEQ ID NO:8)**[[:]]**.

~~T7 promoter~~
~~AGATCTCGATCCCGCGAAATTAATACGACTCACTATAGGGGAATTGTGAGCGGATAACAATTCCCC~~

~~RBS~~
~~TCTAGAAATAATTTTGTTTAACTTTAAGAAGGAGATATACC~~



Please replace paragraph **[0376]** with the following amended paragraph:

[0376] Data collection and refinement statistics for PYK2 kinase domain crystal, and for PYK2 kinase domain/binding compound cocrystal are summarized in the following table:

Data Collection and Refinement Statistics

	Pyk2 (APO)	**Pyk2+AMPPNP**
Crystal Parameters		
Space Group	$P2_1$	$P2_1$
Unit Cell (Å)	a=37.17, b=46.97, c=80.36, [[□]]β=92.63	a=37.32, b=46.98, c=81.11, [[□]]β=92.83
Number of molecules/AU	1	1
V_M (Å^3/Dalton)	2.4	2.4
Solvent content (%)	48	48
Data Collection and Processing		
Resolution (Å)	1.45	1.80
Wavelength (Å)	1.1	1.1
Unique reflections	47843	26149
Redundancy (last shell*)	2.0 (1.8)	4.0 (2.9)
Completeness (last shell) (%)	97.5 (88.9)	99.8 (97.8)
I/[[□]]σ (last shell)	10.9 (1.3)	12.0 (2.3)
R_{sym} (last shell)	0.043 (0.487)	0.063 (0.459)
*Last shell (Å)	1.49 – 1.45	1.85 – 1.80
Refinement		

R_{work} / R_{free} (%)	16.93/20.68	18.62/22.81
Number of Atoms	2583	2507
Rmsd from ideal geometry	0.012 (bond distance), 1.434 (bond angle)	0.010 (bond distance), 1.372 (bond angle)
SigmaA coordinate error	0.16 Å (for 5.0-1.45 Å)	0.14 Å (for 5.0-1.80 Å)
Average B-factors (Å^2)	19.3	20.5
Protein atoms	16.4	19.0
Waters	37.6	34.3
Ligand	-	44.41

Please replace paragraph **[0391]** with the following amended paragraph:

[0391] As an exemplary kinase assay, the kinase activity of PYK2 was measured in AlphaScreening (Packard BioScience). The kinase buffer (HMNB) contains HEPES 50mM at pH7.2, Mg/Mn 5mM each, NP-40 0.1%, and BSA at final 50ug/ml. AlphaScreening is conducted as described by the manufacturer. In brief, the kinase reaction is performed in 384-well plate in 25ul volume. The substrate is biotin-$(E4Y)_3$ **(SEQ ID NO: 27)** at final concentration of 1nM. The final concentration of ATP is 10uM. For compound testing the final DMSO concentration is 1%. The reaction is incubated in 31°C for 1 hour.

Please replace paragraph **[0392]** with the following amended paragraph:

[0392] The Pyk2 kinase domain residues 419 to 691 **(SEQ ID NO: 26)** is an active kinase in AlphaScreen. At a concentration of 8ng/well in 384-well plate, PYK2 shows a Kd of 7.34uM, which is in general agreement with most protein kinases (Table **[[5]]3**). Inhibition by ATP analogs was tested with Pyk2 at 8ng/well and ATP at 10uM. The data is shown in Table **[[5]]3**. The affinity of ATP-g-S and ADP with Pyk2 is at 14uM. Adenosine and AMP-PCP have little effect on PYK2 in the concentration tested.

At page 231, please replace the legend to the final table (i.e., original Table 5, amended Table 3) just before the claims with the following amended legend:

Table **[[5]]3**: Pyk2 Activity and the Inhibition by ATP Analogs